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Synthesis and bioactivity of novel methyl 6-deoxy-6-(*N*′-alkyl/aryl-*N*″-benzothiazol-2-yl)guanidino-α-D-glucopyranosides

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Abstract—A series of new methyl 6-deoxy-6-[*N*′-alkyl/aryl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranosides were obtained from the reaction of an alkyl/aryl amine in the presence of $HgCl_2$ and sugar-thiourea derivatives, followed by the removal of protecting groups. The sugar-thiourea derivatives were obtained from the treatment of 2-aminobenzothiazole derivatives with methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-glucopyranoside in dry pyridine. Some of the synthesized guanidines displayed anti-influenza activity.

Keywords: Sugar isothiocyanate; Sugar-thiourea; Guanidinoglucoside; 2-Aminobenzothiazole; Anti-influenza activity

1. Introduction

The guanidine moiety is of considerable importance as a pharmacophoric group commonly found in many biologically active compounds.[1] Some novel guanidino alkaloids (e.g., ptilomycalin A and the crambescidins, both isolated from marine sponges) are reported to exhibit antiviral activity against herpes simplex virus, antifungal activity against *Candida albicans*, and cytotoxicity against a range of human cancer cell lines, including lung carcinoma A-549, colon carcinoma HT-29, and in vitro against L1210 murine leukemia cells.[2–6] Guanidino-containing sugar and sugar-like molecules also have a wide range of biologically important uses, such as inhibition of replication of HIV,[7] antibacterial activity,[8] treatment of noninsulin-dependent diabetes,[9] antihypertensives,[10] and inhibition of nitric oxide syntheses.[11] A number of benzothiazolyl guanidines have been synthesized and reported to exhibit antibacterial and antitubercular activity.[12] Therefore, the synthesis of guanidino-containing compounds has attracted continued research interests in recent years, and some new efficient synthetic methods and guanidinylation reagents have been used for different classes of guanidine compounds. Typically, the most used guanidinylation protocols employed protected thiourea as guanidinylating reagents and stoichiometric amounts of heavy metal salts such as $HgCl_2$ and $CuCl_2$,[13] $CuSO_4/SiO_2$,[14] PbO,[15] HgO and $AgNO_3$,[16] $Bi(NO_3)_3$ and BiI_3.[17] However, some of these methods showed limited success on account of undesirable conditions and unstable starting materials, especially in the synthesis of guanidino-containing sugars, in which deacetylation was encountered when selectively O-acylated sugar thioureas were used as precursors.

Sugar isothiocyanates rank among the most versatile synthetic intermediates in carbohydrate chemistry.[18] They play a key role in the preparation of a variety of functional groups as well as in the construction of heterocyclic ring systems.[19,20] The reactivity has been widely exploited in the case of glycosyl isothiocyanates, for which several practical syntheses have been developed.[21,22] In contrast, there are few reports on the reactions of carbohydrate derivatives bearing 6-deoxy-6-isothiocyanato functionalities. To broaden the synthesis and bioactivity research of guanidinoglycosides, we used methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-isothiocyanato-α-D-glucopyranoside (**1**) as the starting material,

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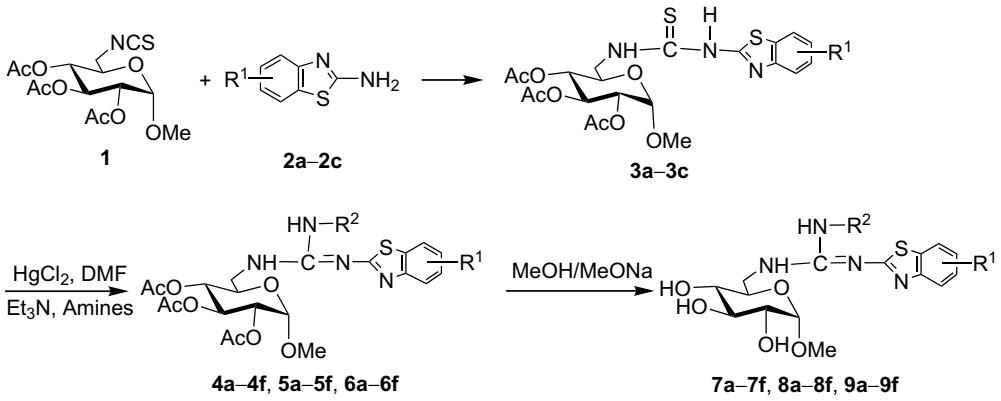

R^1: **4**, **7**: H; **5**, **8**: 6-OCH_3; **6**, **9**: 6-CH_3;

R^2: **a**, *n*-propyl; **b**, *i*-propyl; **c**, cyclohexyl; **d**, *p*-CH_3O-C_6H_4

Scheme 1.

which reacted with 2-aminobenzothiazole derivatives in dry pyridine to give sugar-thioureas (**3a**–**3c**). Treatment of **3a**–**3c** with various amines, and using $HgCl_2$ as a reagent for desulfurization,[13] gave a series of new guanidinoglycoside compounds (Scheme 1). HIV-PR and anti-influenza activity of these compounds have been evaluated, some of which displayed potential biological activities.

2. Results and discussion

2.1. The crystal structure of compound 1 and the synthesis of sugar-thiourea derivatives

Methyl 6-deoxy-6-isothiocyanato-D-glucopyranoside peracetate (**1**) has previously been reported.[23] Its condensation with 2-aminobenzothiazole derivatives in benzene, THF, or $CHCl_3$ by analogy with the preparation of peracetyl glycosylthioureas[24,25] was, however, unsuccessful. Nevertheless, the target sugar-thioureas (**3a**–**3c**) were obtained in high yields when the condensation reaction was performed in dry pyridine. To further understand the important effect of structural factors on their interactions, we investigated the crystal structure of compound **1** and compared it with the data of the reported per-*O*-acetyl D-glucosyl isothiocyanate.[26] Crystal data, structure determination and refinement data of **1** are given in Table 1, and selected bond lengths and bond angles are given in Table 2. The molecular structure of compound **1** with an atomic numbering scheme and a view of the crystal packing down an axis of the compound are shown in Figures 1 and 2, respectively. The bond length of N=C [1.144(5) Å] in the former was found to be shorter than that [1.188(4) Å] in the latter, which implies that the former needs more energy to open the N=C bond in the nucleophilic addition reaction. The

Table 1. Crystal data and structure refinement for the title compound **1**

Empirical formula	$C_{14}H_{19}NO_8S$
Formula weight	361.36
Crystal size	0.60 × 0.54 × 0.48 mm
Crystal system, space group	Orthorhombic, *P* 212121
a (Å)	5.5120(5)
b (Å)	13.8732(12)
c (Å)	23.844(2)
α (°)	90
β (°)	90
γ (°)	90
No. unique reflection	4165
V (Å^3)	1823.4(3)
Z, *D*(calcd) (mg m^{-3})	4, 1.316
Abs. coeff. (mm^{-1})	0.216
F(000)	760
T (K)	253(2)
Limiting indices	$-6 \leqslant h \leqslant 7$, $-17 \leqslant k \leqslant 18$, $-30 \leqslant l \leqslant 30$
R	0.0737
wR	0.2100
Extinction coefficient	0.021(4)
Goodness-of-fit on F^2	1.044
Largest diff. peak and hole	1.291 and −1.002 e Å^{-3}

C=S bond [1.598(4) Å] is longer than that [1.566(3) Å] in the latter, which suggests that this double bond could be opened easily to form the sulfur anion. Pyridine, as a basic solvent, might stabilize the resulting adduct and increase electrophilicity, which is propitious for the nucleophilic additions of amines. The oxygen of the hemiacetal in the latter acts as a strong electron-withdrawing group that enhances the carbon eletrophilicity of the anomeric isothiocyanate, which makes it possible for amines to attack the carbon even in dry benzene, $CHCl_3$, or THF. The point is consistent with the conclusion of Lindhorst and her co-worker in their report, which demonstrated that glycosyl isothiocyanates have higher reactivity than deoxyisothiocyanato sugars.[27]

Table 2. Bond lengths (Å) and angles (°) for the title compound (**1**)[a]

S(1)–C(7)	1.598(4)	O(4)–C(10)	1.349(4)	O(8)–C(5)	1.361(7)	C(2)–C(3)	1.513(4)
O(1)–C(5)	1.426(5)	O(4)–C(3)	1.438(3)	O(8)–C(14)	1.435(6)	C(3)–C(4)	1.507(4)
O(1)–C(1)	1.429(4)	O(5)–C(10)	1.187(4)	N(1)–C(7)	1.144(5)	C(4)–C(5)	1.528(5)
O(2)–C(8)	1.355(4)	O(6)–C(12)	1.350(4)	N(1)–C(6)	1.423(4)	C(8)–C(9)	1.482(5)
O(2)–C(2)	1.449(3)	O(6)–C(4)	1.424(4)	C(1)–C(2)	1.520(4)	C(10)–C(11)	1.494(5)
O(3)–C(8)	1.201(4)	O(7)–C(12)	1.203(4)	C(1)–C(6)	1.521(5)	C(12)–C(13)	1.475(5)
C(5)–O(1)–C(1)	114.0(3)	C(2)–C(1)–C(6)	110.3(3)	O(6)–C(4)–C(5)	111.7(3)	O(3)–C(8)–C(9)	125.9(3)
C(8)–O(2)–C(2)	118.1(2)	O(2)–C(2)–C(3)	105.2(2)	C(3)–C(4)–C(5)	110.2(3)	O(2)–C(8)–C(9)	111.8(3)
C(10)–O(4)–C(3)	118.8(2)	O(2)–C(2)–C(1)	108.7(2)	O(8)–C(5)–O(1)	113.4(4)	O(5)–C(10)–O(4)	124.1(3)
C(12)–O(6)–C(4)	118.0(3)	C(3)–C(2)–C(1)	112.0(2)	O(8)–C(5)–C(4)	108.6(4)	O(5)–C(10)–C(11)	125.9(3)
C(5)–O(8)–C(14)	114.0(7)	O(4)–C(3)–C(4)	108.0(2)	O(1)–C(5)–C(4)	108.2(3)	O(4)–C(10)–C(11)	110.0(3)
C(7)–N(1)–C(6)	159.3(5)	O(4)–C(3)–C(2)	106.5(2)	N(1)–C(6)–C(1)	110.8(3)	O(7)–C(12)–O(6)	122.7(3)
O(1)–C(1)–C(2)	108.9(2)	C(4)–C(3)–C(2)	112.0(3)	N(1)–C(7)–S(1)	176.7(4)	O(7)–C(12)–C(13)	125.3(3)
O(1)–C(1)–C(6)	106.5(3)	O(6)–C(4)–C(3)	106.1(3)	O(3)–C(8)–O(2)	122.3(3)	O(6)–C(12)–C(13)	122.1(3)

[a] Symmetry transformations used to generate equivalent atoms.

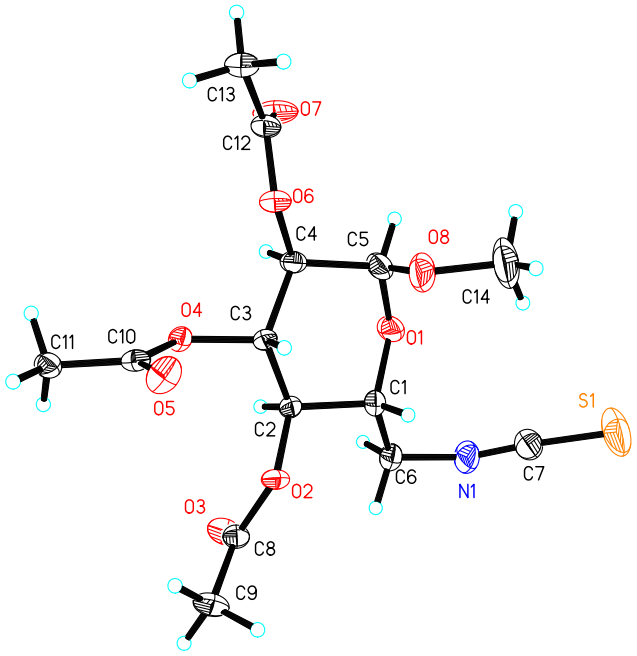

Figure 1. Molecular structure for compound (**1**) with the atomic numbering scheme.

Besides, the control of reaction time and temperature is important, too. We found that it was helpful to improve the yield by properly prolonging the reaction time and increasing the reaction temperature. However, overly long reaction times resulted in the formation of the side product, *N*,*N*′-bis(methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-glucopyranosid-6-yl)thiourea.[28] A clean transformation into the sugar-thioureas (**3a**–**3c**) occurred in five days at 50 °C, with yields of 50–60%. Higher temperatures possibly caused slight formation of deacetylation products that would decrease product purity. Actually, the nucleophilicity of amines determined the degree of the target reaction. 2-Aminobenzothiazole derivatives were more difficult to react with compound **1** than ammonia, alkylamines, and arylamines,[29] due to their π–π and p–π conjugation effects, which decreased the nucleophilicity of the amino group. The results showed that the electron-donating groups on the benzene ring were favorable to the addition reaction, while the reaction of 2-aminobenzothiazole derivatives with electron-withdrawing groups such as chlorine or bromine and compound **1** was not observed.

2.2. The synthesis of guanidinoglucosides

In the course of the guanidinylation, $CuCl_2$, PbO, and $Bi(NO_3)_3$ have been used as guanidinylating agents on account of their low toxicities, but were found to be either ineffective or resulted in poor yields. The desulfurization reaction occurred only under heating, which also caused the deacetylation of the sugar in the alkaline solvent. However, this process was more effective in the presence of $HgCl_2$, which is a more potent desulfurization reagent. When amines reacted with sugar-thioureas (**3a**–**3c**) in the presence of mercuric chloride, guanidinylation did proceed smoothly at room temperature to afford the guanidinoglucosides (**4**–**6**) in 56–77% yield. These were further deacetylated in methanol under standard NaOMe-catalyzed conditions to provide 6-deoxy-6-guanidinoglucosides (**7**–**9**). The incoming amine can be either alkyl or aryl. The reaction was considered to go via a carbodiimide intermediate.[13] However, the guanidines were synthesized in one-step, and carbodiimide intermediates were not isolated in the work.

In fact, mercuric reagents have already been employed in the synthesis of guanidinoglycosides.[30,31] To efficiently convert a thiourea into a guanidine by the $HgCl_2$ protocol, the thiourea should be activated by a strong electron-withdrawing group, and the most general approach to achieve this is by the use of *N*,*N*′-bis-Boc-protected thiourea[13] and *N*-Boc-thiourea.[31,32] Herein, the *N*-benzothiazol-2-yl group actually acts as an alternative activation group for the sugar thiourea in the guanidinylation reaction promoted by $HgCl_2$. The use

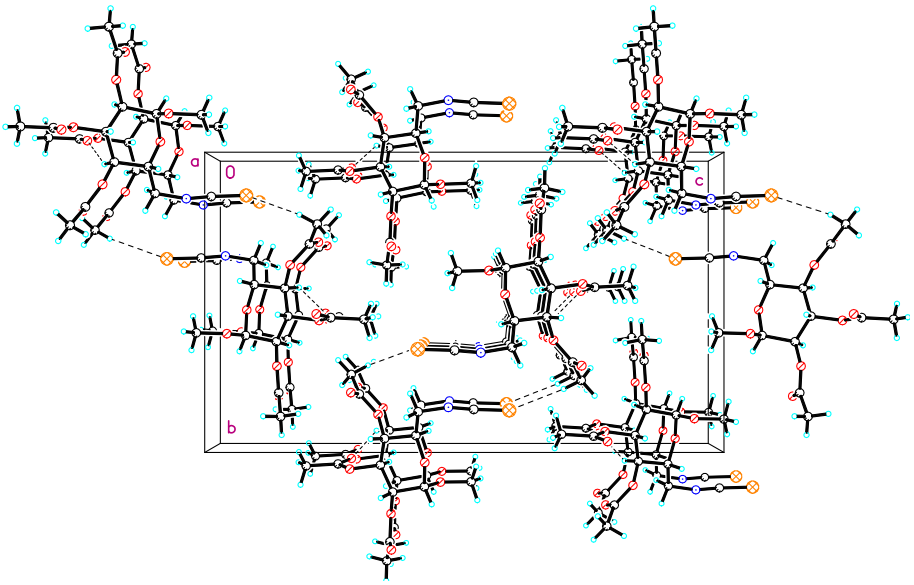

Figure 2. A view of the crystal packing down an axis for compound (**1**).

of *N*,*N*′-bis-Boc-thioureas and *N*-Boc-thioureas can be a drawback by reason of deprotection/protection steps, if guanidines containing different N-substituents need to be synthesized. The limitation can be overcome by using the *N*-benzothiazol-2-yl group. Thus, the $HgCl_2$ method provides a very efficient route to synthesize N,N′,N″-substituted guanidinoglycosides. It is more effective and convenient than the existing methods,[1,9,15] and can result in higher yields.

The structures of new compounds were established by elemental analyses, and by IR, ^1H, and ^{13}C NMR spectroscopy. The LC–ESIMS spectra showed that all the compounds had quasi-molecular ion peaks, most of which were the base peak. It was shown that this type of compound is stable.

2.3. Biological activity

Compounds **4a**, **4d**, **5b**, **6c**, **7a**, **7d**, **8b**, and **9c** were randomly selected to evaluate their anti-influenza virus activity according to the following protocols. Test virus host: MDCK (from dog kidney cells). Positive drug of reference: ribavirin (RBV, Apeloa Pharma Co. of China). Test method: MDCK cells bearing influenza virus B were added to solutions of compounds **4a**, **5b**, **6c**, **4d**, **7a**, **8b**, **9c**, and **7d** in DMSO, then the inhibitory rates of sample on product quantity were tested in unit time. The results are listed in Table 3. Compounds **7a**, **8b**, and **9c** showed anti-influenza virus activity in different concentrations compared with **4a**, **5b**, and **6c**, which implies that hydroxyl groups strongly enhance the inhibition to influenza virus. But, they also displayed higher cytotoxicity than RBV. The HIV-1 protease inhibitory activity of compounds **4a**, **5b**, **6c**, **4d**, **7a**, **8b**, **9c**, and **7d** was also evaluated. The results showed that these compounds were inactive to HIV-1 protease.

In conclusion, we have synthesized a series of new methyl 6-deoxy-6-[*N*′-alkyl/aryl-*N*″-(benzothiazol-2-yl)]-guanidino-α-D-glucopyranosides using the $HgCl_2$–Et_3N protocol. Some of guanidinoglucosides displayed potential biological activities and cytotoxicity. Further studies are in progress to enhance the bioactivity of these compounds by correlating molecular structures with bioactivity.

3. Experimental

3.1. General methods

Melting points were determined on a Yanaco MP-S3 micro melting point apparatus and are uncorrected.

Table 3. Anti-influenza virus activity results of tested compounds

Compound	TC_{50} (μg/ml)[b]	Anti-influenza virus B	
		IC_{50} (μg/ml)[b]	SI[c]
4a	64.15	—[a]	—
5b	160.2	—	—
6c	53.4	—	—
4d	111.11	—	—
7a	160.2	86.23	1.86
8b	192.5	86.23	2.23
9c	9.58	3.19	3.00
7d	28.74	—	—
RBV	384.0	1.23	312.2

[a] '—' means no activity at the biggest nontoxic quantity.

[b] TC_{50}: concentration required to cause 50% death of uninfected MDCK cell; IC_{50}: concentration required to reduce the influenza virus B in MDCK cells by 50%.

[c] SI: selection coefficient, SI = TC_{50}/IC_{50}.

The IR spectra were recorded in KBr pellets on a Bruker FTIR Equinox 55 apparatus. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 400 (using TMS as internal standard). Chemical shifts are expressed as δ units, using $CDCl_3$ and DMSO-d_6 as solvents. The mass spectra were recorded on an HP I000 LC–ESIMS spectrometer. Elemental analyses were performed on a Thermo Flash EA-1112 elemental analyzer. Optical rotation measurements were determined on a Perkin–Elmer 341 polarimeter at 20 °C in $CHCl_3$ solution. Analytical thin-layer chromatography (TLC) was performed on silica gel GF_{254} (Qingdao, China) with EtOAc and light petroleum (fraction boiling in the range of 60–90 °C), and detected by UV light or iodine. Column chromatography was performed on silica gel (100–200 mesh). All reagents were commercial products of analytical grade and were used directly without processing unless noted otherwise. Pyridine was dried over KOH and distilled prior to use. DMF was dried over 4 Å molecular sieves. MeOH was dried over magnesium and distilled prior to use.

3.2. Synthesis of intermediates 1 and 2a–2c

3.2.1. Compound 1 was prepared by the published procedure.[23] mp 100–101 °C, lit.[23] mp 99–100 °C. Transparent colorless crystal of **1** was obtained by slow evaporation over several days from 1:6 EtOAc–hexane solutions.

3.2.2. Compounds 2a–2c were prepared according to the reported method.[33] **2a**: Yield 87%; mp 133–135 °C, lit.[33] mp 131–132 °C; **2b**: Yield 82%; mp 162–164 °C, lit.[33] mp 160–162 °C; **2c**: Yield 83%; mp 134–136 °C, lit.[33] mp 135–136 °C.

3.3. General procedure for the preparation of sugar-thiourea derivatives 3a–3c

An equimolecular mixture of **1** (2 mmol) and 2-aminobenzothiazole derivatives **2a**–**2c** (2 mmol) in 15 mL of dry pyridine was stirred at 50 °C for about 5 days, then concentrated. The residue was purified by silica gel column chromatography using 1:1 EtOAc–petroleum ether as the eluent to give **3a**–**3c**, respectively, as amorphous solids in 52–58% yield.

3.3.1. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-(benzothiazol-2-yl)]thioureido-α-D-glucopyranoside (3a). White solid: yield 572 mg (56%); mp 211–212 °C; $[\alpha]_D^{20}$ +73.1 (*c* 1.0, $CHCl_3$); R_f 0.56; IR (KBr) 3490 (w, NH), 3170 (m, NH), 1749 (s, C=O), 1580, 1525, 1233 and 1036 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.01, 2.09 and 2.10 (3s, each 3H, 3MeCO), 3.40 (s, 3H, OMe), 3.79–3.87 (m, 1H, H-6b), 4.09–4.17 (m, 1H, H-6a), 4.18–4.26 (m, 1H, H-5), 4.92 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.02 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 5.07 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.53 (dd, 1H, $J_{2,3}$ 10.4, $J_{3,4}$ 9.6 Hz, H-3), 7.28–7.75 (m, 4H, ArH), 9.96 (br s, 1H, N′H), 11.40 (br s, 1H, NH); ESIMS: *m*/*z* 512 (100%, $[M+H]^+$), 534 (38%, $[M+Na]^+$). Anal. Calcd for $C_{21}H_{25}N_3O_8S_2$: C, 49.30; H, 4.93; N, 8.21. Found: C, 49.20; H, 4.95; N, 8.11.

3.3.2. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-(6-methoxybenzothiazol-2-yl)]thioureido-α-D-glucopyranoside (3b). White solid: yield 628 mg (58%); mp 180–181 °C; $[\alpha]_D^{20}$ +67.4 (*c* 1.0, $CHCl_3$); R_f 0.39; IR (KBr) 3495 (w, NH), 3172 (m, NH), 1742 (s, C=O), 1585, 1521, 1232 and 1043 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.02, 2.09 and 2.10 (3s, each 3H, 3MeCO), 3.40 (s, 3H, OMe), 3.78–3.85 (m, 1H, H-6b), 3.85 (s, 3H, OMe), 4.08–4.16 (m, 1H, H-6a), 4.16–4.24 (m, 1H, H-5), 4.91 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.02 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 5.06 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.53 (dd, 1H, $J_{2,3}$ 10.0, $J_{3,4}$ 9.6 Hz, H-3), 7.00–7.62 (3H, ArH), 9.97 (br s, 1H, N′H), 11.34 (br s, 1H, NH); ESIMS: *m*/*z* 542 (100%, $[M+H]^+$), 564 (36%, $[M+Na]^+$). Anal. Calcd for $C_{22}H_{27}N_3O_9S_2$: C, 48.81; H, 5.02; N, 7.76. Found: C, 48.69; H, 5.05; N, 7.57.

3.3.3. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-(6-methylbenzothiazol-2-yl)]thioureido-α-D-glucopyranoside (3c). White solid: yield 546 mg (52%); mp 205–206 °C; $[\alpha]_D^{20}$ +65.3 (*c* 1.0, $CHCl_3$); R_f 0.58; IR (KBr) *v*: 3496 (w, NH), 3170 (m, NH), 1749 (s, C=O), 1580, 1524, 1233 and 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.00, 2.08 and 2.12 (3s, each 3H, 3MeCO), 2.40 (s, 3H, CH_3), 3.41 (s, 3H, OMe), 3.42–3.85 (m, 1H, H-6a), 4.07–4.16 (m, 1H, H-6b), 4.17–4.25 (m, 1H, H-5), 4.90 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.00 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 5.04 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.52 (dd, 1H, $J_{2,3}$ 10.4, $J_{3,4}$ 9.6 Hz, H-3), 7.07–7.44 (3H, ArH), 9.95 (br s, 1H, N′H), 11.40 (br s, 1H, NH); ESIMS: *m*/*z* 526 (100%, $[M+H]^+$), 548 (35%, $[M+Na]^+$). Anal. Calcd for $C_{22}H_{27}N_3O_8S_2$: C, 50.27; H, 5.19; N, 7.99. Found: C, 50.16; H, 5.17; N, 7.87.

3.4. General procedure for the preparation of guanidine derivatives 4–6 from thiourea derivatives 3a–3c and alkyl/aryl amines

The starting thiourea (1.0 mmol), amine (1.1 mmol), and Et_3N (3.2 mmol) were dissolved in *N*,*N*-dimethylformamide (5 mL/mmol substrate) at room temperature. The mixture was cooled in an ice bath. Then $HgCl_2$ (1.1 mmol) was added, and the mixture was stirred at 0 °C for 20–50 min. When the color of the reaction mixture changed to black, the reaction was allowed to warm to room temperature. When the reaction was completed (TLC, 2:1 EtOAc–petroleum ether), the reaction mixture was diluted with EtOAc and filtered through Celite,

washing the Celite cake with additional EtOAc. The filtrate was successively washed with brine, satd $NaHCO_3$ solution, and water, dried with $MgSO_4$, and concentrated under reduced pressure to afford a yellow syrup. The crude product thus obtained was further purified by flash chromatography on a silica gel column chromatograph (eluent: 2:1 EtOAc–petroleum ether) to give **4–6**.

3.4.1. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-propyl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (4a). White solid: yield 397 mg (74%); mp 83–85 °C; $[\alpha]_D^{20}$ +72.5 (*c* 1.0, $CHCl_3$); IR (KBr) 3365 (m, NH), 1749 (s, C=O), 1600 (s, guanidino), 1582 (s, aryl), 1225 and 1054 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.06 (t, 3H, CH_3), 1.67–1.78 (m, 2H, CH_2), 2.04, 2.09 and 2.11 (3s, each 3H, 3MeCO), 3.17–3.34 (m, 2H, CH_2), 3.41 (s, 3H, OMe), 3.45–3.61 (br, 1H, H-6a), 3.61–3.76 (br, 1H, H-6b), 3.82 (s, 3H, OMe), 3.93–4.00 (m, 1H, H-5), 4.82 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.93–5.00 (m, 1H, H-4), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.53 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 7.03–7.49 (m, 4H, ArH), 9.60–10.50 (br, 1H, NH), ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9 (C), 170.5, 170.2, 170.1 (C=O), 154.6, 152.0, 131.6, 125.3, 122.1, 120.9, 119.1 (Ar-C), 96.9, 71.1, 70.0, 69.9, 55.1 (OMe), 43.3 (C-6), 42.0 (CH_2), 22.9 (CH_2), 21.0, 20.9, 20.8 (CH_3CO), 13.2 (CH_3). ESIMS: *m*/*z* 537 (100%, $[M+H]^+$), 559 (30%, $[M+Na]^+$). Anal. Calcd for $C_{24}H_{32}N_4O_8S$: C, 53.72; H, 6.01; N, 10.44; Found: C, 53.81; H, 6.03; N, 10.38.

3.4.2. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-isopropyl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (4b). White solid: yield 375 mg (70%); mp 84–86 °C; $[\alpha]_D^{20}$ +70.7 (*c* 1.0, $CHCl_3$); IR (KBr) 3365 (m, NH), 1749 (s, C=O), 1599 (s, guanidino), 1582 (s, aryl), 1225 and 1050 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.24–1.36 (br s, 6H, 2Me), 2.01, 2.09 and 2.12 (3s, each 3H, 3MeCO), 3.41 (s, 3H, OMe), 3.45–3.57 (br, 1H, H-6a), 3.58–3.76 (br, 1H, H-6b), 3.78–4.11 (m, 2H, H-5, CH), 4.86 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.91–5.02 (m, 1H, H-4), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.51 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 7.04–7.64 (m, 4H, ArH), 9.40–10.60 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2 (C), 170.5, 170.3, 170.2 (C=O), 154.8, 152.0, 131.6, 125.3, 122.1, 120.9, 119.1 (Ar-C), 96.9, 71.1, 70.0, 69.9, 55.7 (OMe), 43.3, 41.9, 29.8, 23.4, 21.0, 20.9, 20.8 (CH_3CO); ESIMS: *m*/*z* 537 (100%, $[M+H]^+$), 559 (30%, $[M+Na]^+$). Anal. Calcd for $C_{24}H_{32}N_4O_8S$: C, 53.72; H, 6.01; N, 10.44. Found: C, 53.60; H, 6.03; N, 10.49.

3.4.3. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-cyclohexanyl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (4c). White solid: yield 363 mg (63%); mp 87–89 °C; $[\alpha]_D^{20}$ +64.4 (*c* 1.0, $CHCl_3$); IR (KBr) 3374 (m, NH), 1749 (s, C=O), 1602 (s, guanidino), 1587 (s, aryl), 1225 and 1045 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.24–2.02 (m, 10H, C_5H_{10}), 2.03, 2.07 and 2.12 (3s, each 3H, 3MeCO), 3.32–3.85 (m, 3H, H-6a, H-6b, CH), 3.41 (s, 3H, OMe), 3.94–4.04 (m, 1H, H-5), 4.86 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.91–5.00 (m, 1H, H-4), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.52 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.80–7.48 (m, 4H, ArH), 9.40–10.50 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1 (C), 170.6, 170.5, 170.1 (C=O), 154.6, 152.2, 131.1, 125.0, 122.1, 120.4, 118.4 (Ar-C), 96.7, 71.2, 70.5, 69.9, 69.4, 55.1 (OMe), 50.0 (CH), 43.2 (C-6), 33.4 (CH_2), 29.8 (CH_2), 24.6 (CH_2), 21.5 (CH_2), 21.0, 20.8, 20.4 (CH_3CO); ESIMS: *m*/*z* 577 (100%, $[M+H]^+$), 599 (15%, $[M+Na]^+$). Anal. Calcd for $C_{27}H_{36}N_4O_8S$: C, 56.24; H, 6.29; N, 9.72. Found: C, 56.35; H, 6.25; N, 9.65.

3.4.4. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-(*p*-methoxylphenyl)-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (4d). White solid: yield 336 mg (56%); mp 136–138 °C; $[\alpha]_D^{20}$ +67.1 (*c* 1.0, $CHCl_3$); IR (KBr) 3360 (m, NH), 1753 (s, C=O), 1603 (s, guanidino), 1590 (s, aryl), 1234 and 1038 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.99, 2.07 and 2.15 (3s, each 3H, 3MeCO), 3.29 (s, 3H, OCH_3), 3.49–3.62 (br s, 1H, H-6a), 3.63–3.75 (br s, 1H, H-6b), 3.81–4.01 (m, 1H, H-5), 3.83 (s, 3H, OCH_3), 4.79 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.80–4.85 (m, 1H, H-4), 4.89 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.43 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.82–7.84 (m, 8H, ArH), 10.00–10.80 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5 (C), 170.7, 170.5, 170.2 (C=O), 153.8, 152.4, 150.0, 135.6, 125.4, 122.4, 122.3, 117.6, 113.9 (Ar-C), 96.7, 71.5, 70.2, 69.9, 68.0, 55.7 (OMe), 55.4 (OMe), 42.3 (C-6), 21.0, 20.9 (CH_3CO); ESIMS: *m*/*z* 601 (100%, $[M+H]^+$), 623 (30%, $[M+Na]^+$). Anal. Calcd for $C_{28}H_{32}N_4O_9S$: C, 55.99; H, 5.37; N, 9.33. Found: C, 55.87; H, 5.33; N, 9.28.

3.4.5. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-propyl-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (5a). White solid: yield 402 mg (71%); mp 132–134 °C; $[\alpha]_D^{20}$ +68.3 (*c* 1.0, $CHCl_3$); IR (KBr) 3458 (m, NH), 1742 (s, C=O), 1602 (s, guanidino), 1232 and 1033 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.06 (t, 3H, CH_3), 1.64–1.78 (m, 2H, CH_2), 2.00, 2.09 and 2.12 (3s, each 3H, 3MeCO), 3.16–3.32 (br s, 2H, CH_2), 3.41 (s, 3H, OMe), 3.46–3.61 (br s, 1H, H-6a), 3.61–3.75 (br, 1H, H-6b), 3.82 (s, 3H, OMe), 3.93–4.01 (m, 1H, H-5), 4.85 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.92–5.00 (m, 1H, H-4), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.52 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.85–7.46 (m, 3H, ArH), 9.40–10.50 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2 (C), 170.4, 170.1, 170.1 (C=O), 155.7, 146.5, 132.6, 119.7, 113.4, 104.9 (Ar-C), 96.9, 71.1, 70.1, 69.8, 68.5, 56.0

(OMe), 55.7 (OMe), 43.3 (C-6), 41.9 (CH_2), 22.8, 21.0, 20.9, 20.8 (CH_3CO), 11.7 (CH_3); ESIMS: *m/z* 567 (100%, $[M+H]^+$), 589 (34%, $[M+Na]^+$). Anal. Calcd for $C_{25}H_{34}N_4O_9S$: C, 52.99; H, 6.05; N, 9.89. Found: C, 52.86; H, 6.03; N, 9.85.

3.4.6. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-isopropyl-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (5b). White solid: yield 436 mg (77%); mp 87–89 °C; $[\alpha]_D^{20}$ +67.3 (*c* 1.0, $CHCl_3$); IR (KBr) 3360 (m, NH), 1749 (s, C=O), 1603 (s, guanidino), 1582 (s, aryl), 1225 and 1033 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.20–1.34 (br s, 6H, 2 CH_3), 2.00, 2.05 and 2.12 (3s, each 3H, 3MeCO), 3.42 (s, 3H, OMe), 3.43–3.56 (br s, 1H, H-6a), 3.56–3.78 (br, 1H, H-6b), 3.82 (s, 3H, OMe), 3.78–4.12 (m, 2H, H-5, CH), 4.85 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.90–5.02 (m, 1H, H-4), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.52 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 7.02–7.65 (m, 3H, ArH), 9.50–10.60 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0 (C), 170.6, 170.5, 170.2 (C=O), 156.1, 153.2, 147.2, 131.0, 122.3, 119.2, 105.7 (Ar-C), 97.2, 71.5, 70.8, 69.9, 69.4, 55.6 (OMe), 55.4 (OMe), 43.5, 41.9, 29.9, 23.3 (CH_3), 21.0, 20.9, 20.8 (CH_3CO); ESIMS: *m/z* 567 (100%, $[M+H]^+$), 589 (32%, $[M+Na]^+$). Anal. Calcd for $C_{25}H_{34}N_4O_9S$: C, 52.99; H, 6.05; N, 9.89. Found: C, 52.86; H, 6.05; N, 9.80.

3.4.7. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-cyclohexanyl-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (5c). White solid: yield 430 mg (71%); mp 107–109 °C; $[\alpha]_D^{20}$ +67.3 (*c* 1.0, $CHCl_3$); IR (KBr) 3389 (m, NH), 1749 (s, C=O), 1601 (s, guanidino), 1595 (s, aryl), 1225 and 1038 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.25–2.04 (m, 10H, C_5H_{10}), 2.02, 2.09 and 2.12 (3s, each 3H, 3MeCO), 3.32–3.87 (m, 3H, H-6a, H-6b, CH), 3.41 (s, 3H, OMe), 3.81 (s, 3H, OMe), 3.95–4.04 (m, 1H, H-5), 4.86 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.92–4.98 (m, 1H, H-4), 4.96 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.51 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.80–7.48 (m, 3H, ArH), 9.45–10.50 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1 (C), 170.6, 170.5, 170.0 (C=O), 155.8, 153.6 (C), 146.5, 135.4, 122.0, 117.4, 105.6 (Ar-C), 96.4, 71.3, 70.0, 69.9, 68.6, 55.7 (OMe), 55.4 (OMe), 47.8 (CH), 41.2 (C-6), 33.7 (CH_2), 25.3 (CH_2), 24.2 (CH_2), 21.0, 20.8, 20.4 (CH_3CO); ESIMS: *m/z* 607 (100%, $[M+H]^+$), 629 (17%, $[M+Na]^+$). Anal. Calcd for $C_{28}H_{38}N_4O_9S$: C, 55.43; H, 6.31; N, 9.23. Found: C, 55.28; H, 6.33; N, 9.29.

3.4.8. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-(*p*-methoxylphenyl)-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (5d). White solid: yield 302 mg (48%); mp 141–142 °C; $[\alpha]_D^{20}$ +62.8 (*c* 1.0, $CHCl_3$); IR (KBr) 3365 (m, NH), 1751 (s, C=O), 1601 (s, guanidino), 1595 (s, aryl), 1227 and 1037 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.00, 2.07 and 2.10 (3s, each 3H, 3MeCO), 3.29 (s, 3H, OCH_3), 3.51–3.62 (br s, 1H, H-6a), 3.63–3.76 (br s, 1H, H-6b), 3.81–4.00 (m, 1H, H-5), 3.83 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.78 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.81–4.85 (m, 1H, H-4), 4.88 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.45 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.85–7.50 (m, 7H, ArH), 11.22–11.42 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6 (C), 170.4, 170.3, 170.1 (C=O), 158.5, 155.8, 153.9, 146.1, 132.6, 128.4, 120.0, 115.3, 113.6, 104.9 (Ar-C), 96.7, 71.1, 70.2, 69.8, 68.3, 55.9 (OMe), 55.7 (OMe), 55.4 (OMe), 41.3 (C-6), 21.0, 20.9 (CH_3CO); ESIMS: *m/z* 631 (100%, $[M+H]^+$), 653 (28%, $[M+Na]^+$). Anal. Calcd for $C_{29}H_{34}N_4O_{10}S$: C, 55.23; H, 5.43; N, 8.88. Found: C, 55.32; H, 5.40; N, 8.78.

3.4.9. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-propyl-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyr anoside (6a). White solid: yield 413 mg (75%); mp 125–127 °C; $[\alpha]_D^{20}$ +67.5 (*c* 1.0, $CHCl_3$); IR (KBr) 3360 (m, NH), 1740 (s, C=O), 1601 (s, guanidino), 1589 (s, aryl), 1225 and 1038 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.06 (t, 3H, CH_3), 1.66–1.78 (br s, 2H, CH_2), 2.00, 2.09 and 2.12 (3s, each 3H, 3MeCO), 2.40 (s, 3H, CH_3), 3.14–3.36 (m, 2H, CH_2), 3.41 (s, 3H, OMe), 3.47–3.64 (br, 1H, H-6a), 3.64–3.88 (br, 1H, H-6b), 3.93–4.05 (m, 1H, H-5), 4.85 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.91–5.02 (m, 1H, H-4), 4.97 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.51 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 7.04–7.50 (m, 3H, ArH), 9.70–10.30 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6 (C), 170.6, 170.2, 170.1 (C=O), 155.3 (C), 150.1, 131.6, 130.9, 127.3, 121.1, 118.1 (Ar-C), 96.3, 71.0, 70.6, 69.9, 55.3 (OMe), 43.1 (C-6), 41.3 (CH_2), 25.3, 20.9, 20.8 (CH_3CO), 18.4 (CH_3), 13.6 (CH_3); ESIMS: *m/z* 551 (100%, $[M+H]^+$), 573 (31%, $[M+Na]^+$). Anal. Calcd for $C_{25}H_{34}N_4O_8S$: C, 54.53; H, 6.22; N, 10.18. Found: C, 54.58; H, 6.20; N, 10.10.

3.4.10. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-isopropyl-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (6b). White solid: yield 402 mg (73%); mp 101–102 °C; $[\alpha]_D^{20}$ +68.8 (*c* 1.0, $CHCl_3$); IR (KBr) 3356 (m, NH), 1749 (s, C=O), 1601 (s, guanidino), 1590 (s, aryl), 1230 and 1053 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.24–1.35 (m, 6H, 2 CH_3), 2.00, 2.08 and 2.12 (3s, each 3H, 3MeCO), 2.40 (s, 3H, CH_3), 3.45–3.58 (br, 1H, H-6a), 3.59–3.76 (br, 1H, H-6b), 3.78–4.11 (m, 2H, H-5, CH), 4.86 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.93–5.02 (m, 1H, H-4), 4.97 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.51 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 7.03–7.64 (m, 3H, ArH), 9.45–10.60 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4 (C), 170.5, 170.3, 170.2 (C=O), 154.8, 152.0 (C), 132.1, 130.5, 126.9, 120.9, 118.5 (Ar-C), 97.5, 71.6, 70.0, 69.9, 68.0, 55.4 (OMe), 42.8 (C-6), 41.5 (CH), 23.4 (CH_2),

21.0, 20.9, 20.7 (CH_3CO), 18.3 (CH_3); ESIMS: *m*/*z* 551 (100%, $[M+H]^+$), 573 (35%, $[M+Na]^+$). Anal. Calcd for $C_{25}H_{34}N_4O_8S$: C, 54.53; H, 6.22; N, 10.18. Found: C, 54.66; H, 6.20; N, 10.10.

3.4.11. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-cyclohexanyl-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (6c). White solid: yield 372 mg (63%); mp 94–95 °C; $[\alpha]_D^{20}$ +62.2 (*c* 1.0, $CHCl_3$); IR (KBr) 3375 (m, NH), 1748 (s, C=O), 1602 (s, guanidino), 1589 (s, aryl), 1225 and 1053 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.20–2.02 (m, 10H, C_5H_{10}), 2.00, 2.08 and 2.12 (3s, each 3H, 3MeCO), 2.39 (s, 3H, CH_3), 3.32–3.88 (m, 3H, H-6a, H-6b, CH), 3.40 (s, 3H, OMe), 3.93–4.02 (m, 1H, H-5), 4.86 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.89–5.04 (m, 1H, H-4), 4.97 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.50 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.95–7.45 (m, 3H, ArH), 9.40–10.50 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6 (C), 170.5, 170.2, 170.2 (C=O), 155.3, 153.0, 131.9, 131.6, 126.5, 121.0, 118.2 (Ar-C), 96.8, 71.2, 70.1, 69.9, 68.8, 55.7 (OMe), 49.9 (CH), 42.3 (C-6), 33.2 (CH_2), 30.0 (CH_2), 25.7 (CH_2), 24.4 (CH_2), 21.5 (CH_2), 21.0, 20.9, 20.8 (CH_3CO), 18.4 (CH_3); ESIMS: *m*/*z* 591 (100%, $[M+H]^+$), 613 (16%, $[M+Na]^+$). Anal. Calcd for $C_{28}H_{38}N_4O_8S$: C, 56.93; H, 6.48; N, 9.49. Found: C, 56.81; H, 6.46; N, 9.40.

3.4.12. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[*N*′-(*p*-methoxylphenyl)-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (6d). White solid: yield 344 mg (56%); mp 120–122 °C; $[\alpha]_D^{20}$ +64.2 (*c* 1.0, $CHCl_3$); IR (KBr) 3400 (m, NH), 1750 (s, C=O), 1603 (s, guanidino), 1592 (s, aryl), 1230 and 1037 (s, C–O–C) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.01, 2.05 and 2.09 (3s, each 3H, 3MeCO), 2.40 (s, 3H, CH_3), 3.32 (s, 3H, OCH_3), 3.52–3.63 (br s, 1H, H-6a), 3.63–3.77 (br s, 1H, H-6b), 3.82–4.01 (m, 1H, H-5), 3.83 (s, 3H, OCH_3), 4.79 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 4.82–4.84 (m, 1H, H-4), 4.87 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.46 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 6.82–7.84 (m, 7H, ArH), 10.00–10.82 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5 (C), 170.7, 170.5, 170.2 (C=O), 155.8, 153.4, 150.2, 146.0, 135.6, 132.8, 122.4, 117.3, 115.6, 114.3, 103.6 (Ar-C), 96.4, 71.3, 70.2, 69.9, 68.0, 55.9 (OMe), 55.4 (OMe), 41.6 (C-6), 21.0, 20.9 (CH_3CO), 18.6 (CH_3); ESIMS: *m*/*z* 615 (100%, $[M+H]^+$), 637 (26%, $[M+Na]^+$). Anal. Calcd for $C_{29}H_{34}N_4O_9S$: C, 56.67; H, 5.58; N, 9.11. Found: C, 56.58; H, 5.54; N, 9.09.

3.5. General procedure for the preparation of methyl 6-deoxy-6-guanidino-α-D-glucopyranoside (7–9)

To a solution of the corresponding guanidines (**4**–**6**) (0.05 mmol) in MeOH (5 mL) was added NaOMe (0.1 M, 0.1 mL), and the reaction mixture was stirred at room temperature for 2.5–5 h when TLC (9:1 CH_3Cl–MeOH) revealed complete consumption of the starting material. The reaction mixture was crystallized on standing at 4 °C, or some water was added to promote crystallization. The solution was filtered and washed with water to give the crude product, which was recrystallized from 90% alcohol to give the deacetylated guanidines **7**–**9**.

3.5.1. Methyl 6-deoxy-6-[*N*′-propyl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (7a). White solid: yield 185 mg (90%); mp 142–143 °C; $[\alpha]_D^{20}$ +52.4 (*c* 1.0, DMSO); IR (KBr) 3389 (s, NH, OH), 1603 (s, guanidino), 1559, 1486 and 1047 (s, C–O–C) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 0.91 (t, 3H, CH_3), 1.52–1.58 (m, 2H, CH_2), 3.20–3.30 (m, 2H, CH_2), 3.33 (s, 3H, OMe), 3.37–3.48 (m, 1H, H-6a), 3.50–3.64 (m, 2H, H-5, H-6b), 4.62 (s, 1H, H-2), 4.85 (t, 1H, H-4), 4.91 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 5.23 (d, 1H, H-3), 6.74 (br s, 1H, N′H), 7.06–7.47 (m, 4H, ArH), 9.71 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.1 (C), 154.3, 152.1, 131.4, 124.7, 124.4, 119.3, 119.1 (Ar-C), 100.8, 73.4, 72.1, 70.7, 69.9, 55.1 (OMe), 43.3 (C-6), 43.0, 21.5, 12.3; ESIMS: *m*/*z* 411 (100%, $[M+H]^+$), 433 (37%, $[M+Na]^+$). Anal. Calcd for $C_{18}H_{26}N_4O_5S$: C, 52.67; H, 6.38; N, 13.65. Found: C, 52.61; H, 6.35; N, 13.48.

3.5.2. Methyl 6-deoxy-6-[*N*′-propyl-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (8a). White solid: yield 210 mg (95%); mp 228–229 °C; $[\alpha]_D^{20}$ +46.7 (*c* 1.0, DMSO); IR (KBr) 3378 (s, NH, OH), 1603 (s, guanidino), 1575 and 1047 (s, C–O–C) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 0.90 (t, 3H, CH_3), 1.52–1.57 (m, 2H, CH_2), 3.18–3.28 (m, 2H, CH_2), 3.34 (s, 3H, OMe), 3.39–3.52 (m, 1H, H-6a), 3.53–3.65 (m, 2H, H-5, H-6b), 3.76 (s, 3H, OMe), 4.61 (s, 1H, H-2), 4.84 (t, 1H, H-4), 4.91 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 5.24 (d, 1H, H-3), 6.73 (br s, 1H, N′H), 7.00–7.45 (m, 3H, ArH), 9.72 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.4 (C), 156.1, 151.1, 145.3, 134.6, 122.3, 119.1, 104.5 (Ar-C), 101.3, 73.4, 72.2, 71.0, 69.2, 55.7 (OMe), 55.4 (OMe), 43.2 (C-6), 43.0, 21.4, 12.2; ESIMS: *m*/*z* 441 (100%, $[M+H]^+$), 463 (36%, $[M+Na]^+$). Anal. Calcd for $C_{19}H_{28}N_4O_6S$: C, 51.80; H, 6.41; N, 12.72. Found: C, 51.74; H, 6.39; N, 12.61.

3.5.3. Methyl 6-deoxy-6-[*N*′-propyl-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (9a). White solid: yield 189 mg (89%); mp 226–227 °C; $[\alpha]_D^{20}$ +52.3 (*c* 1.0, DMSO); IR (KBr) 3376 (s, NH, OH), 1600 (s, guanidino), 1573 and 1047 (s, C–O–C) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 0.91 (t, 3H, CH_3), 1.52–1.58 (m, 2H, CH_2), 2.32 (s, 3H, CH_3), 3.20–3.30 (m, 2H, CH_2), 3.38–3.47 (m, 1H, H-6a), 3.34 (s, 3H, OMe),

3.52–3.64 (m, 2H, H-5, H-6b), 4.62 (s, 1H, H-2), 4.85 (t, 1H, H-4), 4.93 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 5.22 (d, 1H, H-3), 6.77 (br s, 1H, N′H), 7.04–7.24 (m, 3H, ArH), 9.74 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.5 (C), 156.2, 150.3, 131.5, 131.0, 127.0, 121.3, 118.5 (Ar-C), 100.6, 73.6, 72.6, 70.7, 55.1 (OMe), 43.2, 43.1, 23.1, 21.5, 12.0; ESIMS: *m/z* 425 (100%, $[M+H]^+$), 447 (16%, $[M+Na]^+$). Anal. Calcd for $C_{19}H_{28}N_4O_5S$: C, 53.76; H, 6.65; N, 13.20. Found: C, 53.81; H, 6.60; N, 13.25.

3.5.4. Methyl 6-deoxy-6-[*N*′-isopropyl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (7b). White solid: yield 169 mg (82%); mp 146–148 °C; $[\alpha]_D^{20}$ +54.2 (*c* 1.0, DMSO); IR (KBr) 3378 (s, NH, OH), 1601 (s, guanidino), 1589 and 1047 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.16 (d, 6H, $2CH_3$), 3.21–3.29 (m, 1H, H-6a), 3.35 (s, 3H, OMe), 3.38–3.46 (m, 1H, CH), 3.50–3.64 (m, 2H, H-5, H-6b), 4.65 (s, 1H, H-2), 4.89 (d, 1H, H-4), 4.92 (d, 1H, $J_{1,2}$ 4.8 Hz, H-1), 5.24 (d, 1H, H-3), 6.45 (br s, 1H, N′H), 7.02–7.50 (m, 4H, ArH), 9.75 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.4 (C), 154.5, 153.1, 134.6, 125.4, 125.2, 120.9, 120.7 (Ar-C), 100.3, 73.2, 72.8, 71.2, 69.9, 55.4 (OMe), 43.2, 42.8, 23.2, 21.5; ESIMS: *m/z* 411 (100%, $[M+H]^+$), 433 (34%, $[M+Na]^+$). Anal. Calcd for $C_{18}H_{26}N_4O_5S$: C, 52.67; H, 6.38; N, 13.65. Found: C, 52.65; H, 6.36; N, 13.60.

3.5.5. Methyl 6-deoxy-6-[*N*′-isopropyl-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (8b). White solid: yield 172 mg (78%); mp 160–162 °C; $[\alpha]_D^{20}$ +51.5 (*c* 1.0, DMSO); IR (KBr) 3368 (s, NH, OH), 1603 (s, guanidino), 1591 and 1047 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.15 (d, 6H, $2CH_3$), 3.22–3.29 (m, 1H, H-6a), 3.35 (s, 3H, OMe), 3.38–3.48 (m, 1H, CH), 3.50–3.65 (m, 2H, H-5, H-6b), 3.75 (s, 3H, OMe), 4.66 (s, 1H, H-2), 4.85 (d, 1H, H-4), 4.93 (d, 1H, $J_{1,2}$ 4.8 Hz, H-1), 5.26 (d, 1H, H-3), 6.45 (br s, 1H, N′H), 7.01–7.46 (m, 3H, ArH), 9.73 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.6 (C), 156.1, 153.2, 147.5, 131.0, 122.3, 114.8, 104.3 (Ar-C), 100.4, 73.5, 72.5, 70.6, 69.4, 55.7 (OMe), 55.3 (OMe), 43.5, 42.7, 23.3, 21.5; ESIMS: *m/z* 441 (100%, $[M+H]^+$), 463 (35%, $[M+Na]^+$). Anal. Calcd for $C_{19}H_{28}N_4O_6S$: C, 51.80; H, 6.41; N, 12.72. Found: C, 51.68; H, 6.38; N, 12.76.

3.5.6. Methyl 6-deoxy-6-[*N*′-isopropyl-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (9b). White solid: yield 172 mg (81%); mp 178–180 °C; $[\alpha]_D^{20}$ +51.9 (*c* 1.0, DMSO); IR (KBr) 3365 (s, NH, OH), 1601 (s, guanidino), 1589 and 1047 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.16 (d, 6H, $2CH_3$), 2.32 (s, 3H, CH_3), 3.22–3.30 (m, 1H, H-6a), 3.35 (s, 3H, OMe), 3.38–3.47 (m, 1H, CH), 3.50–3.65 (m, 2H, H-5, H-6b), 4.65 (s, 1H, H-2), 4.88 (d, 1H, H-4), 4.93 (d, 1H, $J_{1,2}$ 4.8 Hz, H-1), 5.24 (d, 1H, H-3), 6.46 (br s, 1H, N′H), 7.01–7.46 (m, 3H, ArH), 9.72 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.4 (C), 155.4, 150.3, 131.5, 131.0, 127.0, 121.3, 118.5 (Ar-C), 100.6, 73.6, 72.6, 70.7, 55.2 (OMe), 43.2, 42.8, 23.4, 23.3, 21.5; ESIMS: *m/z* 425 (100%, $[M+H]^+$), 447 (36%, $[M+Na]^+$). Anal. Calcd for $C_{19}H_{28}N_4O_5S$: C, 53.76; H, 6.65; N, 13.20. Found: C, 53.63; H, 6.62; N, 13.24.

3.5.7. Methyl 6-deoxy-6-[*N*′-cyclohexanyl-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (7c). White solid: yield 203 mg (90%); mp 202–203 °C; $[\alpha]_D^{20}$ +50.0 (*c* 0.9, DMSO); IR (KBr) 3374 (s, NH, OH), 1602 (s, guanidino), 1576 and 1046 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.05–1.92 (m, 10H, 5 CH_2), 3.23–3.30 (m, 1H, H-6a), 3.33 (s, 3H, OMe), 3.38–3.47 (m, 1H, CH), 3.47–3.65 (m, 2H, H-5, H-6b), 4.64 (s, 1H, H-2), 4.87 (s, 1H, H-4), 4.92 (s, 1H, H-1), 5.27 (s, 1H, H-3), 6.44 (br s, 1H, N′H), 7.04–7.46 (m, 4H, ArH), 9.75 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.3 (C), 155.5, 150.2, 135.1, 125.0, 122.1, 122.0 (Ar-C), 99.9, 72.5, 71.9, 69.5, 69.0, 55.1 (OMe), 50.1, 44.2, 33.7, 25.6, 21.6; ESIMS: *m/z* 451 (100%, $[M+H]^+$), 473 (14%, $[M+Na]^+$). Anal. Calcd for $C_{21}H_{30}N_4O_5S$: C, 55.98; H, 6.71; N, 12.44. Found: C, 55.92; H, 6.74; N, 12.49.

3.5.8. Methyl 6-deoxy-6-[*N*′-cyclohexanyl-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (8c). White solid: yield 214 mg (89%); mp 223–225 °C; $[\alpha]_D^{20}$ +36.7 (*c* 1.0, DMSO); IR (KBr) 3368 (s, NH, OH), 1602 (s, guanidino), 1585 and 1046 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.02–1.95 (m, 10H, 5 CH_2), 3.24–3.30 (m, 1H, H-6a), 3.32 (s, 3H, OMe), 3.38–3.48 (m, 1H, CH), 3.49–3.65 (m, 2H, H-5, H-6b), 3.76 (s, 3H, OMe), 4.62 (s, 1H, H-2), 4.87 (s, 1H, H-4), 4.91 (d, 1H, $J_{1,2}$ 4.8 Hz, H-1), 5.26 (s, 1H, H-3), 6.43 (br s, 1H, N′H), 7.00–7.50 (m, 3H, ArH), 9.73 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.1 (C), 154.8, 153.2, 145.1, 135.5, 122.2, 113.1, 104.1 (Ar-C), 100.5, 73.3, 72.6, 70.9, 69.2, 55.1 (OMe), 53.0 (OMe), 47.3, 42.9, 33.2, 27.5, 22.2; ESIMS: *m/z* 481 (100%, $[M+H]^+$), 503 (16%, $[M+Na]^+$). Anal. Calcd for $C_{22}H_{32}N_4O_6S$: C, 54.98; H, 6.71; N, 11.66. Found: C, 55.03; H, 6.69; N, 11.60.

3.5.9. Methyl 6-deoxy-6-[*N*′-cyclohexanyl-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (9c). White solid: yield 213 mg (92%); mp 212–213 °C; $[\alpha]_D^{20}$ +40.5 (*c* 1.0, DMSO); IR (KBr) 3369 (s, NH, OH), 1602 (s, guanidino), 1576 and 1046 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.05–1.95 (m, 10H, 5 CH_2), 2.33 (s, 3H, CH_3), 3.17–3.37 (m, 1H, H-6a), 3.34 (s, 3H, OMe), 3.37–3.47 (m, 1H, CH), 3.47–3.65

(m, 2H, H-5, H-6b), 4.63 (s, 1H, H-2), 4.87 (s, 1H, H-4), 4.91 (s, 1H, H-1), 5.27 (s, 1H, H-3), 6.43 (br s, 1H, N′H), 7.00–7.51 (m, 3H, ArH), 9.72 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.4 (C), 161.9, 155.2, 150.1, 131.6, 130.9, 127.1, 121.4, 118.6, 113.5 (Ar-C), 100.5, 73.3, 72.4, 70.8, 63.0, 55.1 (OMe), 49.6, 43.0, 33.1, 25.8, 25.5, 21.5; ESIMS: m/z 465 (100%, $[M+H]^+$), 487 (16%, $[M+Na]^+$). Anal. Calcd for $C_{22}H_{32}N_4O_5S$: C, 56.88; H, 6.94; N, 12.06. Found: C, 56.81; H, 6.89; N, 12.00.

3.5.10. Methyl 6-deoxy-6-[*N*′-(*p*-methoxylphenyl)-*N*″-(benzothiazol-2-yl)]guanidino-α-D-glucopyranoside (7d). White solid: yield 181 mg (76%); mp 127–129 °C; $[\alpha]_D^{20}$ +52.8 (*c* 1.0, DMSO); IR (KBr) 3374 (s, NH, OH), 1609 (s, guanidino), 1570 and 1046 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.34 (s, 3H, OMe), 3.38–3.54 (m, 1H, H-6a), 3.54–3.65 (m, 1H, H-6b), 3.68–3.86 (m, 1H, H-5), 3.76 (s, 3H, OMe), 4.67 (s, 1H, H-2), 4.88 (s, 1H, H-4), 4.93 (d, 1H, $J_{1,2}$ 4.4 Hz, H-1), 5.27 (d, 1H, J 5.2 Hz, H-3), 6.86–7.74 (m, 8H, ArH), 8.59 (br s, 1H, N′H), 10.00 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.8 (C), 156.8 (C), 154.7, 152.0, 131.1 126.1, 122.7, 121.6, 119.2, 114.5 (Ar-C), 100.6, 73.6, 72.6, 70.5, 55.9 (OMe), 55.2 (OMe), 43.7 (C-6); ESIMS: m/z 475 (100%, $[M+H]^+$), 497 (32%, $[M+Na]^+$). Anal. Calcd for $C_{22}H_{26}N_4O_6S$: C, 55.68; H, 5.52; N, 11.81. Found: C, 55.54; H, 5.53; N, 11.79.

3.5.11. Methyl 6-deoxy-6-[*N*′-(*p*-methoxylphenyl)-*N*″-(6-methoxybenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (8d). White solid: yield 217 mg (86%); mp 198–199 °C; $[\alpha]_D^{20}$ +46.5 (*c* 1.0, DMSO); IR (KBr) 3376 (s, NH, OH), 1607 (s, guanidino), 1578 and 1047 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.34 (s, 3H, OMe), 3.37–3.54 (m, 1H, H-6a), 3.55–3.65 (m, 1H, H-6b), 3.69–3.86 (m, 1H, H-5), 3.76 (s, 3H, OMe), 3.78 (s, 3H, OMe), 4.67 (s, 1H, H-2), 4.88 (s, 1H, H-4), 4.92 (d, 1H, $J_{1,2}$ 4.4 Hz, H-1), 5.28 (d, 1H, J 5.2 Hz, H-3), 6.86–7.73 (m, 7H, ArH), 8.58 (br s, 1H, N′H), 10.01 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.1 (C), 155.9, 153.2, 150.2, 146.5, 135.5, 122.8, 118.6, 117.6, 113.2, 106.2 (Ar-C), 100.6, 73.6, 72.4, 70.9, 69.5, 55.9 (OMe), 55.7 (OMe), 55.4 (OMe), 43.9 (C-6); ESIMS: m/z 505 (100%, $[M+H]^+$), 527 (32%, $[M+Na]^+$). Anal. Calcd for $C_{23}H_{28}N_4O_7S$: C, 54.75; H, 5.59; N, 11.10. Found: C, 54.79; H, 5.57; N, 11.06.

3.5.12. Methyl 6-deoxy-6-[*N*′-(*p*-methoxylphenyl)-*N*″-(6-methylbenzothiazol-2-yl)]guanidino-α-D-glucopyranoside (9d). White solid: yield 190 mg (78%); mp 199–201 °C; $[\alpha]_D^{20}$ +48.2 (*c* 1.0, DMSO); IR (KBr) 3369 (s, NH, OH), 1602 (s, guanidino), 1576 and 1047 (s, C–O–C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.33 (s, 3H, CH_3), 3.32 (s, 3H, OMe), 3.38–3.55 (m, 1H, H-6a), 3.55–3.65 (m, 1H, H-6b), 3.68–3.88 (m, 1H, H-5), 3.76 (s, 3H, OMe), 4.67 (s, 1H, H-2), 4.88 (s, 1H, H-4), 4.92 (d, 1H, $J_{1,2}$ 4.4 Hz, H-1), 5.28 (d, 1H, J 5.2 Hz, H-3), 6.90–7.72 (m, 7H, ArH), 8.58 (br s, 1H, N′H), 10.00 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0 (C), 153.4, 151.2, 150.6, 136.3, 132.4, 130.8, 127.4, 121.1, 120.9, 119.3, 115.7 (Ar-C), 100.2, 73.5, 72.6, 70.8, 69.7, 60.0 (OMe), 55.1 (OMe), 43.6 (C-6), 21.3 (CH_3); ESIMS: m/z 489 (100%, $[M+H]^+$), 511 (35%, $[M+Na]^+$). Anal. Calcd for $C_{23}H_{28}N_4O_6S$: C, 56.54; H, 5.78; N, 11.47. Found: C, 56.45; H, 5.76; N, 11.39.

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Supplementary data

Complete crystallographic data for the structural analysis of compound **1** have been deposited with the Cambridge Crystallographic Data Centre, CCDC numbers 659968. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. (telephone: +44-01223-762910, facsimile: +44-01223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2007.12.001.

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